MULTIPLE DIFFUSE FIBROSARCOMA OF BONE*

PAUL E. STEINER, M.D.
(From the Department of Pathology, The University of Chicago, Chicago, Ill.)

In 1936 I encountered a malignant tumor of the skeleton which defied classification. The case was submitted to the Bone Sarcoma Registry of the American College of Surgeons where it stands recorded (no. 2032) as unique. A number of experienced American and European bone pathologists who studied the tumor expressed interesting views, some of which will be given; none had seen a similar tumor. Because it presents several features which are new for bone tumors, it is reported at this time.

Histologically the tumor was a fairly innocent-appearing, long spindle-celled fibrosarcoma of not uncommon appearance. The unusual features consisted of the manner of its growth and of its distribution in the skeleton in association with this histological type. It was widely distributed in bones, which it destroyed. Its disposition was essentially that of the reticulo-endothelial and hemopoietic tissues in the bone marrow of adults. Nowhere did it form any considerable mass or enlargement suggestive of a primary site of origin. There were small metastases in the viscera.

While tumors with this distribution and behavior are not rare, being characteristic of the myelomas, the association of these features with the cytology encountered in this case is unusual.

REPORT OF CASE

L. D., white, male, 43 years old, who was employed as a coal passer on a railroad, was a patient of Dr. L. H. Sloan † at the Illinois Central Hospital, Chicago. Except for dryness and scaling of the skin of the extremities the patient was well until 1934, when he began to have pain in his back. There was no history of trauma. He continued to work until December, 1935, when his back pain became too severe for him to continue, and he entered the hospital on January 16, 1936. The pain was mostly lumbar. It was continuous, did not radiate and was worse at night and on motion.

On the first physical examination the back appeared normal. The left leg was shorter than the right and the pelvis was tilted. The left knee jerk was increased. The left testicle was atrophic. Other findings were normal except for ichthyosis of the skin of the arms and back.

Routine examinations of the blood, urine and stools at this time were negative, as were a gastric analysis and Wassermann and Kahn tests on the blood and spinal fluid.

A lateral roentgenogram of the lumbar vertebra showed no evidence of fracture, dislocation, demineralization, or other bone abnormality. Fluoroscopic examination

* Received for publication, November 23, 1943.

† I am indebted to Dr. Sloan for permission to report this case and to Dr. William Culpepper for the roentgenograms.

of the thorax and its viscera disclosed no abnormality. The esophagus, stomach and duodenum were negative for filling defects when examined after a barium meal, and, except for marked ptosis of the transverse colon, the lower intestinal tract was not remarkable.

On January 28, 1936, a moderate bowing of the spine to the right in the dorsal region and a lordosis in the lumbar region were noted. The left leg was shortened and both femurs were slightly bowed.

The diagnosis at this time was possible beginning Paget's disease.

The patient resumed work on February 1, 1936, but he was unable to continue and he returned to the hospital on May 5, 1936, where he remained until his death on October 30, 1936. He continued to have severe pain in the lower dorsal and lumbar regions. It was not relieved by removal of all of his teeth, traction, or by drugs which later included narcotics. His dorsal and lumbar spine now became fixed, and there was a kyphos in the region of the 8th dorsal vertebra.

On July 28th a neurological examination was negative. Spinal puncture yielded clear fluid with a cell count of 12. A guinea-pig injected with this fluid did not develop tuberculosis. On July 29th new roentgenographic studies showed ". . . . a destructive process involving the bodies of the 4th, 5th, 6th and 9th thoracic vertebrae and the 1st lumbar vertebral body; also the transverse processes; the 12th rib on the left side and the 11th right rib, suggestive of malignancy. Mottled appearance of the pelvis suggestive of atrophic changes is present."

During August two small nodules appeared on the ribs, and in September non-traumatic fractures of the 6th, 7th and 8th ribs were noted. Numbness to the level of the knees developed in September. The urine showed albumin occasionally but was negative for Bence-Jones protein in August and in October. The patient had a severe progressive anemia. The pulse was constantly rapid. During May and June there was a daily afternoon fever with peaks at 99° to 100° F. Early in July a bout of fever with temperatures up to 102° F. was followed by temperatures at the former level. His appetite was poor and he had frequent emeses. Pain was intense. He became dyspneic in October, grew weaker and expired on October 30, 1936. There was no x-ray or radium therapy.

The final clinical impression was that of a malignant tumor metastatic to bone, with the primary site undetermined.

Abstract of Necropsy Examination

The final anatomical diagnoses were: Multiple, diffuse fibrosarcomas of bones; extensive fibrosarcomatous invasion and destruction of the spine with kyphoscoliosis; fibrosarcomatous invasion and destruction of the sternum, ribs, clavicles, pelvis, upper ends of the humeri and femurs, sphenoid and parietal bones; fibrosarcomatous metastases to the lungs, liver, spleen, heart, pancreas, kidneys and adrenals; marked emaciation and anemia; brown atrophy of the heart and liver; generalized serous atrophy of fat; multiple cutaneous nevi; ichthyosis; atrophy of the right kidney and compensatory hypertrophy of the left; slight adenomatous hyperplasia of the adrenals; atrophy of the left testis; traction diverticulum of the esophagus; accessory spleen.

External Appearance. The body was that of an extremely emaciated, deformed and pale white male appearing about 55 years of age rather than the stated 43 years. The estimated weight was 100 lbs. and the

estimated length, 70 inches. The skin showed a marked ichthyosis, being thick, dry, branny and scaling. It was finely cracked and large shreds of dry epidermis could be pulled off almost anywhere. The skin also showed many flat, soft, pale brownish nevi up to 1 cm. in diameter. They were numerous on the trunk, both anteriorly and posteriorly, several dozen being visible. None appeared malignant on gross examination.

The body was deformed. The skull was large. The zygomatic arches were prominent, and the clavicles were very conspicuous. The sternum was deformed, having a deep transverse depression at the level of the junction of manubrium and body and another groove across the lower end of the body. The entire sternum, therefore, lay near the spine, and the chest was flat and long. The costal cartilages were concave and the costochondral junctions were knob-like. Several ribs had small fusiform swellings.

The extremities were wasted. The left leg was about 2 inches shorter than the right. The spine had several abnormal curvatures which will be described with the skeleton.

Body Cavities. Except that the upper two-thirds of the right lung was everywhere adherent to the parietal pleura by fibrous adhesions, the great body cavities appeared normal. The adipose tissue was scanty and dark.

Esophagus. At the level of the tracheal bifurcation there was a diverticulum of the esophagus which admitted half of the distal phalanx of the index finger. Externally it was firmly adherent to a scarred tracheobronchial lymph node.

Parathyroids. The parathyroids appeared about normal in size. They measured: Right upper, 4 by 3 by 1.5 mm.; right lower, 5 by 4 by 2 mm.; left lower, 4 by 4 by 1.5 mm.; left upper, 7 by 4 by 2 mm.

Heart. The heart weighed 300 gm. The epicardial fat was gelatinous and dark, the myocardium was brown and the endocardium was unusually opaque.

Lungs. Each lung had a number of flat, button-like, grayish white, neoplastic pleural nodules up to 1.5 cm. in diameter and not over 2 mm. thick. They had red margins. Scattered throughout the substance of all lobes were numerous hard, grayish white nodules up to 1 cm. in diameter. Similar tumors enclosed and thickened the walls of many bronchi.

Liver. The liver weighed 1510 gm. Through the thin capsule 15 to 18 firm whitish neoplastic nodules up to 2.5 cm. in diameter were visible. The larger tumors had umbilicated centers. Similar tumors were seen throughout the liver substance.

Spleen. The spleen weighed 190 gm. Under the capsule on the diaphragmatic surface there was a nodule, 8 mm. in diameter, and several smaller tumors were visible on the surfaces made by cutting.

Pancreas. One nodule, 4 mm. in diameter, was seen on the anterior surface of the pancreas.

Adrenals. The adrenals were enlarged, together weighing 17.5 gm. One had a yellow nodular area, 2 mm. in size, in the cortex. The other was diffusely enlarged by an infiltration of grayish white tumor, growing in both the cortex and medulla.

Kidneys. The left kidney was markedly atrophic, weighing 31 gm. Its artery was small but not occluded. The right kidney weighed 140 gm. Two firm, whitish nodules of neoplasm, measuring 1.2 and 0.3 cm., were seen in it.

Generative Organs. The left testis was small and fibrotic, while the right appeared normal. The seminal vesicles and the prostate were not remarkable.

Muscular System. The muscles were atrophic and pale. The fat and connective tissue around the muscles was gelatinous, resembling that of serous atrophy.

Skeleton. The calvarium was hard and thinner than usual. An osteolytic tumor, 1.5 cm. in diameter, had eroded both tables in the left parietal bone. The sphenoid was soft and largely replaced by firm, yellowish gray, neoplastic tissue, although its configuration was retained.

The spine showed a number of abnormal curves. In the lower cervical region it turned backward and to the left, forming a kyphoscoliosis, with a sharp angle in the upper dorsal region. It then overcompensated by passing to the right in the lower dorsal region. In the lumbar spine was another kyphoscoliosis to the left. The pelvis was tilted, and it was higher on the left. There were no visible or palpable abnormalities in the bones of the pelvis.

With the knife a wedge-shaped segment was cut from the vertebral column, which appeared comparatively normal externally except for the abnormal curves already described. This wedge of bone was removed with ease from the cervical region to the sacrum. Examination then disclosed that the vertebral bodies were almost entirely replaced by firm, yellowish white tumor. Consequently they were very soft (Fig. 4). Some of the vertebral bodies had collapsed so that they were narrower than the intervertebral disks.

The sternum was angulated and deformed, as previously described. Pieces could be cut from it with ease with the knife at any point (Fig.

4). Both cortex and marrow spaces appeared to be replaced by tumor, although the bone was not enlarged.

The ribs lay near each other because of the partial collapse of the spine and the sinking of the sternum. They could be bent and fractured with ease, and they could be cut with the knife (Fig. 4). The 5th, 6th and 7th left ribs showed slight fusiform enlargements at the sites of previous fractures.

When the lower end of the upper third of the left femur was opened it was found to be of normal hardness. The cortex was thick and the marrow cavity was small. One small neoplastic nodule was seen eroding the cortex from within at this level (Fig. 4).

No bony enlargement resembling a primary tumor site was seen anywhere in the skeleton.

Post-mortem Roentgenograms. Because all bones could not be examined thoroughly at necropsy, post-mortem roentgenograms were made of the trunk, legs and humeri. The femurs showed outward bowing and irregular osteolytic lesions in the center of the upper third, head and neck. Each femur showed a few sharp, osteolytic lesions, about 3 mm. in diameter, in the upper part, but the bones of the leg below this level showed no abnormality. The remainder of the skeleton, except for the distal two-thirds of each clavicle, showed marked demineralization and deformities as described. The cortex of the bones was greatly thinned or entirely absent. Numerous, irregular, confluent osteolytic lesions in each bone were responsible for the osteoporosis.

Histopathology

Only those histopathologic changes which are considered pertinent will be described.

The Tumor. The tumor was composed of spindle cells which, in the sections of bone, were long and slender, but which, in the visceral metastases, were more pleomorphic, although the spindle form was dominant. The nuclei in general were spindle-shaped, but some were irregular. They were usually of medium size but a few giant forms were seen. The chromatin was slightly clumped and scanty, and some hyperchromatic nuclei were found. Mitotic figures were few. The cytoplasm was poorly seen because it was slight in amount and because of the large amount of intercellular fibrillar and mucinous material. The fibrils stained like collagen by the van Gieson, Mallory, and Masson methods. With the Mallory phosphotungstic acid-hematoxylin stain the fibrils were seen to be predominantly adjacent to and not in the cell cytoplasm. Silver impregnation by Perdau's method revealed

much reticulum in the more cellular parts of the tumor. Collagen was abundant in all sections but the greatest amounts were found in the sections of bone. The stroma in many places had a bluish, mucoid appearance, but such regions stained poorly or not at all with mucicarmine.

The cells grew, in general, in the form of broad bundles, but in a few places they had an irregular, whorl-like growth, and elsewhere the growth was even and diffuse. The tumor contained few blood vessels. There was no necrosis. Nowhere did it form bone or cartilage, and no definite osteoid tissue was seen. A fine brown pigment was seen in the tumor in the liver, spleen and bone marrow. This gave a positive Prussian blue reaction for iron and it failed to react positively with Masson's silver impregnation method for melanin. Since a similar pigment was found in these locations apart from the tumor, it was not considered significant.

Bones. The neoplastic growth in many sections of the bones completely replaced the marrow, from which it appeared to have arisen. It destroyed trabeculae and cortex, eroding through the latter in many places. In such places it elevated the periosteum but little or not at all, and it stimulated no periosteal new bone. While occasional tumor cells infiltrated the surrounding soft parts in a few places, no extracortical tumors were formed and the configuration and size of the bones was remarkably well preserved. The tumor was osteolytic, apparently by direct action as well as by stimulation of osteoclasts. Small pieces of necrotic bone enclosed by tumor were found. At one point was seen some calcification in dense collagen.

Vertebral Body. Both cortical and cancellous bone was almost completely destroyed by the tumor, which was here very fibrous. The tumor cells infiltrated the intervertebral disks. Small calcospherites (possibly artifacts) were numerous.

Rib. At this point the rib was almost entirely replaced by tumor, although islands of cortex persisted. There was no sign of repair in an old fracture.

Sternum. Here also was seen total replacement of the bone marrow and nearly complete destruction of the bone itself. Although, as elsewhere, tumor cells penetrated the periosteum, they failed to form extra-osseous tumor masses.

Femur. At the lower end of the upper third of the femur there was a solitary, osteolytic neoplastic nodule, 1 cm. in diameter, eroding the cortex from within. From this point tumor cells were infiltrating the marrow spaces and into the haversian canals. Osteoclasts were

exceptionally numerous here. Elsewhere this bone and its marrow were normal, the latter showing active hemopoiesis.

Visceral Metastases. In the viscera the metastases were fairly sharply circumscribed but infiltrative. The tumor cells tended to invade the surrounding tissues and to incorporate some of the more resistant structures within their limits.

Adrenals. A noncircumscribed metastasis was present in an adrenal. This centered in the medulla and reticular zone, and grew out between the cells of the fascicular zone in delicate linear rows. Another section showed a nodular area composed of atypically arranged cortical cells.

Heart. The endocardial opacity seen grossly was found to be due to an infiltration of the subendocardial region by metastatic tumor, which also extended into the myocardium, particularly along the perivascular connective tissue. A papillary muscle was sheathed by a similar growth.

Lungs. The tumor formed flat masses in the pleura, sheathed some of the blood vessels and bronchi, and infiltrated into the surrounding lung. In some places an exceptionally large amount of mucoid stroma was found.

Liver. In the liver the tumor formed distinct nodules in which the cells showed the greatest degree of pleomorphism and the most whorling.

Spleen. The metastases were poorly circumscribed and highly infiltrative in the spleen.

Kidney. The tumor infiltrated the kidney parenchyma and included the remains of kidney structures. Numerous small metastases, not seen grossly, were present. The stroma was very mucinous, even in the smallest metastases.

Pancreas. One small metastasis was seen in the pancreas.

Miscellaneous. Brief reference is made to additional structures in which no metastases were found.

Parathyroids. No abnormality was seen in the parathyroids except that the oxyphil cells were possibly more numerous than usual at this age.

Skin. There was marked hyperkeratosis and some follicular plugging of the skin. Aside from this the epidermis was very thin, in some places being only six cells thick. The papillae were slender, long, sometimes clubbed and occasionally connected. There was an irregular increase in melanin. The dermis contained a collection of nonpigmented nevus cells. There was no fibrosis or inflammation of the dermis.

Discussion

In summary, this was a purely osteolytic, slightly anaplastic fibrosarcoma which was widely disseminated throughout the hemopoietic and reticulo-endothelial areas of the skeleton, where it replaced the bones without causing enlargement suggestive of a primary site. There were small metastases in many viscera. In addition there was ichthyosis.

Two views about the nature of this tumor present themselves. One is that it represents widespread sarcomatous change in Paget's disease. The other is that it is a peculiar fibrosarcoma probably arising from the medulla of bone and possibly multicentric in origin, and thus related to the myelomas, which it resembles in its distribution and behavior. While it is impossible, from the available evidence, to decide between these two theories, it is my opinion that the latter explanation is more probable. Evidence for both views, and others, will be presented, together with the opinions expressed by some of the consultants.

The main reasons for considering the diagnosis of Paget's disease with sarcomatous change are the pelvic deformity and the bowing of the femurs. The roentgenograms show a change which might be interpreted as new bone formation above the acetabulum, in the trochanters and on the concave side of the femurs.

Against the diagnosis of osteitis deformans is the failure of any section of bone to show the changes characteristic of this disease. There is no new bone formation and the fibrotic tissue can all be regarded as fibrosarcoma. The skull was thin and hard. The tibia showed no roentgenographic changes, and nowhere else are the films typical for this disease. The bones were not thickened or deformed. Furthermore, extensive Paget's disease is unlikely at this age.

Additional reasons for considering this to be a bone sarcoma which arose independently of Paget's disease are its rapid course of 10 months, counting from the time a physician was first consulted. In January roentgenograms were negative and in July destructive lesions were well advanced. At no time were the roentgenographic changes characteristic of Paget's disease.

The question as to whether this tumor was solitary or multicentric in origin cannot be settled at the present time any more than it can with plasma cell or other myelomas. The fact that on the first roentgenographic examination of the skeleton no lesions were found, while 6 months later they were widespread, indicates either simultaneous origin in many places or rapid metastasis. The apparent origin, almost simultaneously, in many bones and the absence of one lesion larger than the others suggest multicentric origin. Multiple, independent

primary tumors in bone, other than myelomas, have been described but they are not common. The distribution in the skeleton, namely, that of the hemopoietic and reticulo-endothelial marrow, cannot be used as evidence either way, because it is common to myelomas and to extensive neoplastic metastasis to bones from within or from without the skeleton.

The presence of marked skin changes, here called ichthyosis, which preceded the development of the bone sarcoma is of interest. No causal relationship has been established between these two conditions, but neither has this possibility been excluded. The thick, dry, scaling skin was stated to have been present for many years, and it became worse as the cancer cachexia developed.

In view of the marked skin changes, as well as some profound alterations in the connective tissues, leading in the connective tissue of bone to sarcoma, a nutritional disturbance, possibly in the nature of vitamin deficiencies, was suspected. No positive evidence for such factors could be found. No history of past dietary deficiencies, indiscretions, or food likes and dislikes could be elicited.

The question also arises as to the relationship, if any, of the nevi in the skin to the osseous sarcoma. Could this be an example of widespread melanosarcoma metastatic into bone, or could it be an extensive disorder of the neuro-ectoderm with nevi in the skin and neurogenic sarcoma in bone? There are good reasons for rejecting the first of these hypotheses: None of the nevi appeared malignant, the cytological appearance of the tumor was not that of melanosarcoma, and there was no melanin in the cells, even by special staining methods. The second idea is less easily disposed of, but neither is there any strong evidence in its favor. While neurogenic sarcomas commonly consist of a spindle-celled growth with whorling, scattered giant cells and a tendency to mucinous degeneration in the stroma, they do not have any known special affinity for the skeleton, either as primary tumors or as metastases. A generalized neurosarcomatosis of the skeleton has not been described to my knowledge, but localized cases have been described. Also, in most areas, the tumor did not resemble the structure of neurogenic sarcoma but was more like that of the ordinary fibrosarcoma. The skeletal changes sometimes seen in cases of von Recklinghausen's neurofibromatosis are unlike those in the present case.

Several consultants, in their reports which are quoted below, emphasized a point which has not hitherto been stressed, namely, that some of the lesions, even in viscera, appeared more like independent foci giving rise to sarcoma than like metastases. This idea is based

on the diffuse, highly infiltrative nature of such areas. There is, however, no gradual gradation from nonneoplastic to sarcomatous connective tissue cells at the margins of such areas but only admixture of these two types of cells. In my opinion the situation is analogous to that found in some carcinomas of the pancreas in which areas are found which appear to consist of precancerous epithelial cells, although probably such is not the case. Grossly, in the present example, the visceral tumors appeared like ordinary metastases. They were distinctly circumscribed.

Excerpts from the written opinions of several consultants are as follows:

Dr. Fred W. Stewart wrote: "I . . . . do not recognize any known disease. Some of the visceral lesions are consistent with metastases but some are not. The fine interstitial fibroses in lung, heart, kidney and adrenal seem part of a general morbid change in connective tissues. The clinical association with extreme ichthyosis is at least remarkable if we merely throw it into the category of Paget's, especially since the bone lesions are not classical of Paget's, nor is extensive Paget's apt to occur at 43."

Dr. E. A. Codman expressed the opinion that: "My best guess is that this is an instance of Paget's disease in which the osteolytic phase far exceeds the osteogenic. . . . The marrow spaces in Paget's disease always show fibrosis. In this instance the fibrosis, by its superlative character, becomes a generalized new growth, just as in many cases of Paget's disease in which a localized sarcoma forms. In this case the process seems to be diffuse. . . . The metastases resemble those in cases of osteogenic sarcoma arising in Paget's disease, *i.e.*, they are nondescript and not very characteristic of having arisen in the bone. I see no evidence to indicate whether the metastases in this case arose from a single tumor or from different foci, but I believe there is evidence of diffuse malignant changes in several bones."

Dr. James Ewing wrote in part: "This case is quite peculiar and I do not remember anything like it. There are some features resembling spindle cell medullary sarcoma of the sclerosing type such as one sees in the medulla of long bones. These features are origin in the medulla, spindle cell structure, osteolytic tendency, absence of bone production and cellular areas suggesting a capacity to give metastases. The multiple tumors may be explained as metastases, but this origin is far from clear. The distribution especially about the spine and in the sternum is very peculiar and suggests rather a primary multiple origin, which is unknown with sclerosing spindle cell bone sarcoma. I do not see enough of the features of Paget's disease to warrant one in including

the case among the sarcomas arising in this disease, where, however, it may possibly belong. The most peculiar and significant feature is the apparent beginning of the proliferative process in organs outside of bone, as adrenal, heart muscle and lung. Here the process is not that of a metastatic lesion, but one finds the very earliest stages of proliferation of spindle cells about fine blood vessels, especially in heart muscle and adrenal. These lesions suggest an universal tendency to proliferation of perithelial cells similar to that seen in some forms of vitamin deficiency. What is the meaning of the extensive ichthyosis of the skin? This has certainly nothing to do with Paget's disease and indicates the presence of some general nutritional dyscrasia."

Dr. Kurt Apitz of the University of Berlin expressed the following opinion and stated that it was that also of Professor Hamperl: "This is—as you rightly put it in your diagnosis—a generalized sarcomatosis of the bones and viscera. The histologic appearance of the tumor is roughly that of a fibrosarcoma, but in its finer details it is quite unusual. I have not seen before such a regular whirl-like arrangement of collagen fibres, except in neurogenic tumors; but the latter origin has little probability for other reasons. I rather think the tumor might be derived from periosteal tissue. If the primary is small, it is quite possible that you cannot differentiate it from the widespread metastatic growth. The sections of the bones are very interesting because they show a peculiar type of calcification, a slight tendency towards osteoid formation, and intensive osteoclastic bone destruction. I do not see how the diagnosis of Paget's disease could be justified. There is only overwhelming metastasis in the marrow, and no other newly formed fibrous tissue, and there is no new bone with mosaic structures."

Summary

An osteolytic fibrosarcoma of bone is described in which the lesions appeared at approximately the same time in many bones, and in which the tumors, although highly infiltrative, retained the normal configuration of the bones. The distribution and extent of the sarcoma was that of the hemopoietic and reticulo-endothelial areas in the skeleton. There were small metastases in many viscera. It is believed that this is an example of a medullary fibrosarcoma somewhat analogous to the myelomas, and that it, like them, might have had a multicentric origin.

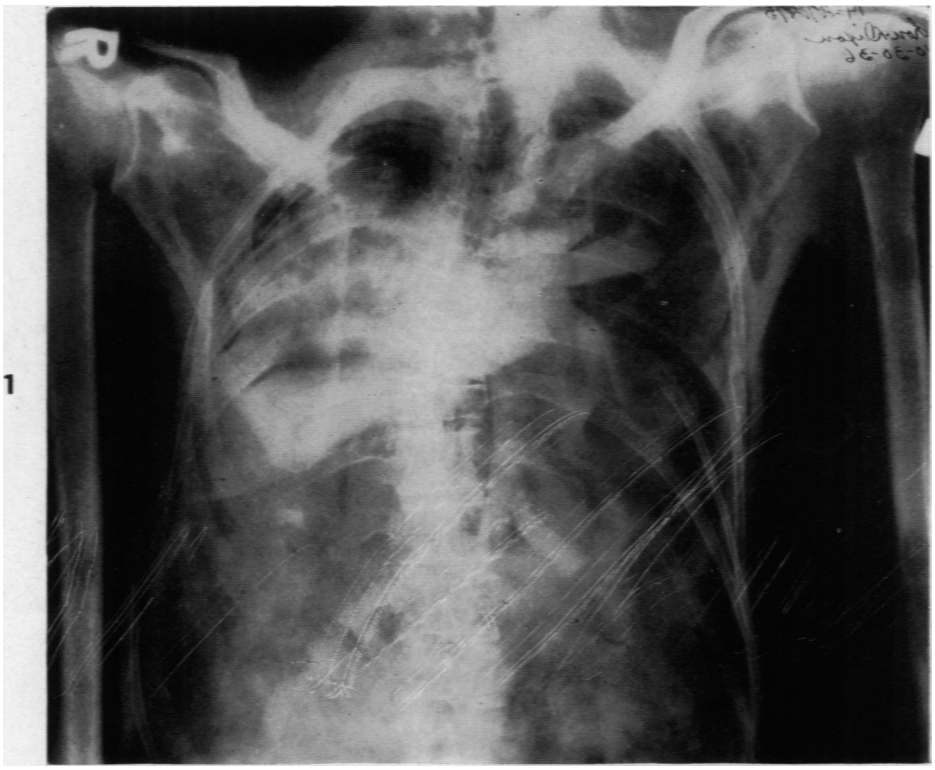
[*Illustrations follow*]

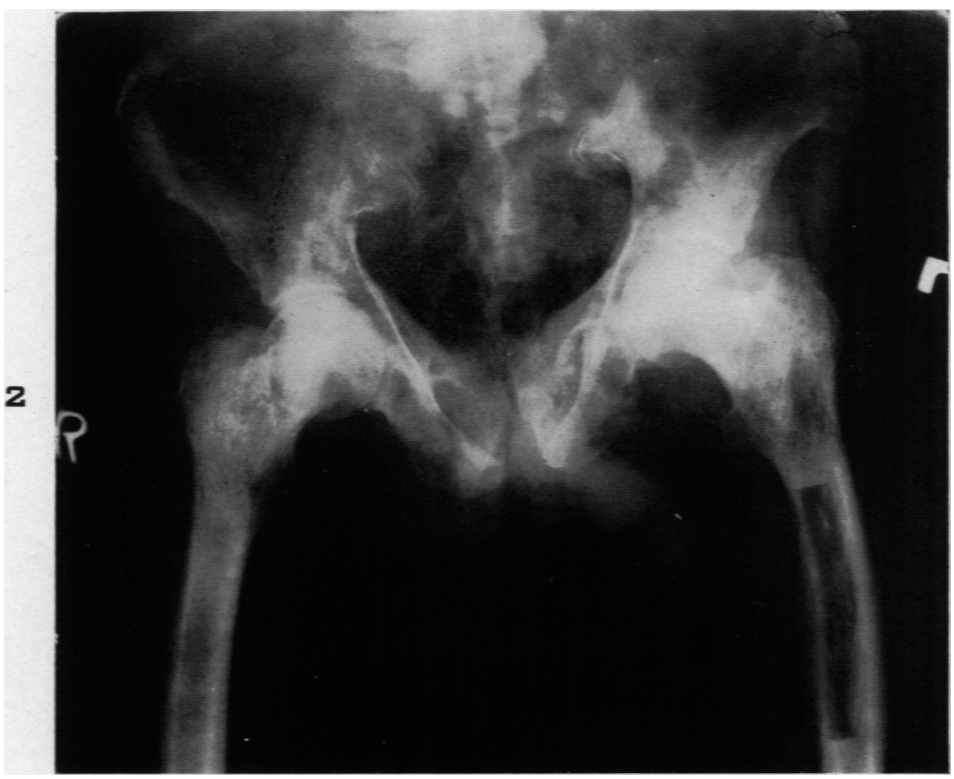
DESCRIPTION OF PLATES

PLATE 157

FIG. 1. Post-mortem roentgenogram showing osteolytic lesions in the humeri, ribs, spine and scapulae. Segments of two upper left ribs were removed and are shown in detail in the lower center of Figure 4.

FIG. 2. Post-mortem roentgenogram showing destructive lesions in the sacrum, pelvis and femora together with slight bowing of the latter. The bone fragment removed from the left femur is shown in Figure 6.





Steiner Multiple Diffuse Fibrosarcoma of Bone

PLATE 158

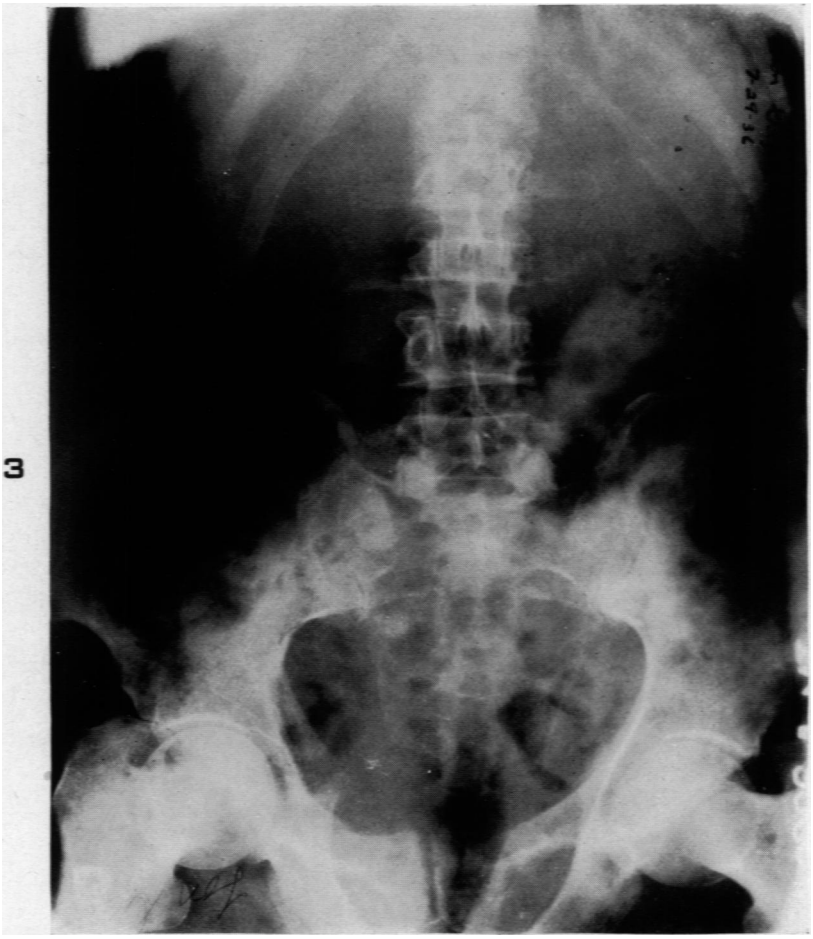
FIG. 3. Post-mortem roentgenogram of the lower spine and pelvis, showing osteolytic lesions.

FIG. 4. Roentgenogram of a segment of spine showing marked focal and diffuse bone destruction with collapse of several vertebral bodies, and retention of the normal osseous configuration; also (lower left) a segment from the center of the sternum, two left upper ribs (lower center), and a segment of the left femur (lower right), which, by contrast, is underexposed.

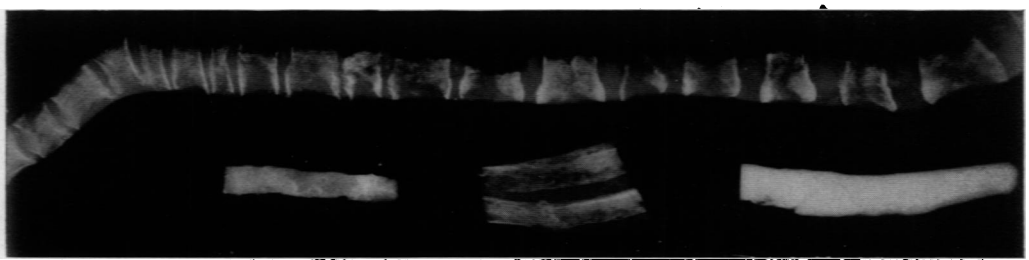
FIG. 5. Portion of liver showing numerous metastases. These were the largest of the visceral metastases.

FIG. 6. Segment of cortex of the left femur showing one osteolytic lesion.

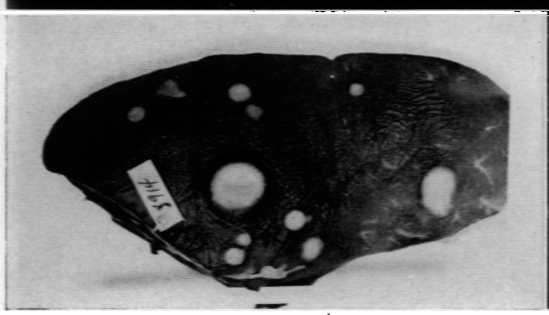
3

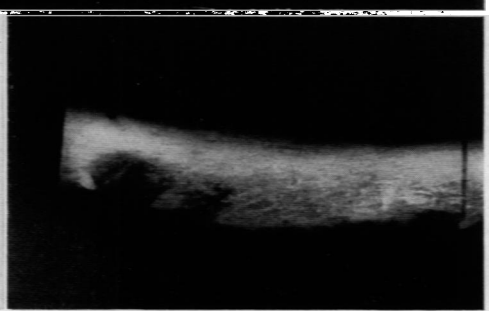


4



5





6

Steiner Multiple Diffuse Fibrosarcoma of Bone

PLATE 159

FIG. 7. Photomicrograph through the center of the sternum showing replacement of the marrow by tumor, partial destruction of trabeculae of bone and invasion, with focal penetration of the cortex and periosteum. × 20.

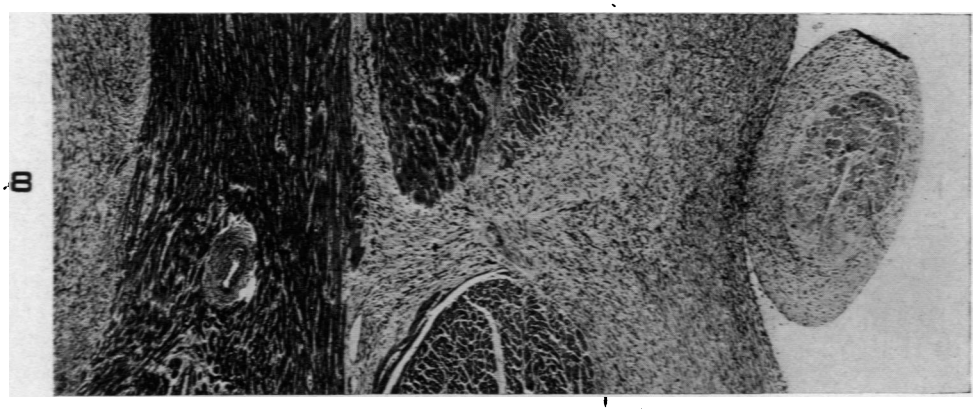
FIG. 8. Tumor metastasis to the heart. A papillary muscle is enclosed by tumor which also replaces the endocardium and invades the myocardium. × 42.

FIG. 9. High power photomicrograph showing the details of the tumor cells in the sternal bone marrow. × 395.

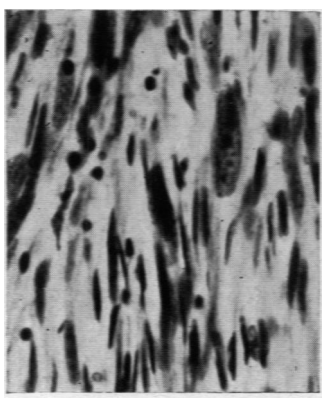
FIG. 10. Lower power photomicrograph showing the most anaplastic and pleomorphic growth which the tumor exhibited. This was in the liver. × 225.

FIG. 11. The manner of tumor infiltration through the adrenal. Similar growth was seen in the pancreas, kidneys and spleen. × 225.

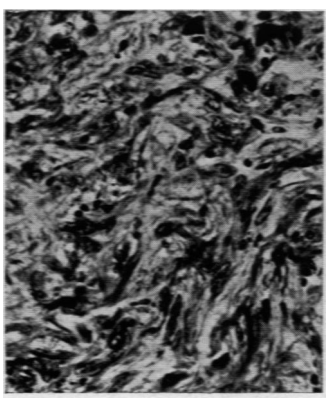
7



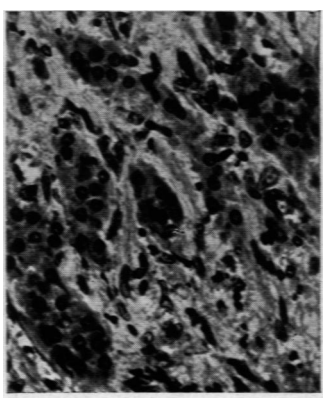
8



9



10



11

Steiner Multiple Diffuse Fibrosarcoma of Bone